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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/894,788 08/27/97 GIACOMONI

HM22/0921

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EXAMINER

ART UNIT	CHANN	PAPER	NUMBER
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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Paper No. 29

Application Number: 08/894,788
Filing Date: August 27, 1997
Appellant(s): GIACOMONI, PAOLO

Michelle E. O'Brien
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's reply brief on appeal filed on 8-21-01.

Grounds of Rejection

Claim Rejections - 35 U.S.C. § 103

Claims 31-38, 40-54 and 56-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over

1) Hahn et al in view of Williamson et al; or 2) Hahn et al in view of Wahl et al; or 3) Hahn et al
in view of Williamson et al and Wahl et al.

Art Unit: 1615

Hahn teaches a number of substances, which when applied topically can cause skin irritation. The substances include vehicles in which active ingredients are formulated (carriers), solvents, detergents, fragrances, propellants, salicylic acid derivatives, retinoids etc., and cause irritation which ranges from mild irritation to severe dermatitis conditions. Further, Hahn teaches that people with sensitive skin has an inherent predisposition to skin irritants, for example, people with skin conditions such as psoriasis, contact dermatitis etc., (see col. 3, lines 27-43). Hahn teaches the theory that an anti-irritant, to counteract the irritants, can be used together with an irritant, in the same composition. Hahn teaches strontium cation as an anti-irritant (see entire document, particularly, cols. 1-4, 10 and 11), but fails to teach the claimed nitric oxide (NO) synthase inhibitor as anti-irritant.

However, Williamson teaches NO synthase inhibitors, such as like methyl-, dimethyl or amino substituted guanidines, for the treatment of chronic and acute inflammatory conditions (column 2, lines 44-54; col. 3, lines 13-18). Williamson also recognizes N-monomethyl-L-arginine, as a NO synthase inhibitor (col. 1, lines 60-65). The acute and chronic inflammatory conditions taught by Williamson include dermatitis, drug reactions, sunburn, insect bites, burns (thermal, chemical and electrical) (column 3, lines 38-45). Williamson et al also teaches pharmaceutically acceptable diluents and carriers (see col. 11, lines 35-39), which according to Hahn et al are capable of producing skin irritation.

A skilled artisan would be motivated to incorporate any anti-irritant, in the place of strontium cation in the teachings of Hahn et al, and still be able to counteract the irritation. NO synthase inhibitors of Williamson et al are capable of inhibiting chronic and acute dermatitis, a skin condition caused by chemicals (which according to Hahn et al is caused due to irritation by

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various chemical substances). Therefore, it would have been obvious for a skilled artisan to substitute the strontium cation of Hahn et al with NO synthase inhibitors of Williamson et al, with an expectation to inhibit the irritation by caused by the substances of Hahn et al.

Williamson does not teach topical application of nitric oxide synthase inhibitor. However, applying nitric oxide synthase inhibitors of Williamson et al as a topical formulation would have been obvious from the teachings of Hahn et al, or alternatively, it is within the scope of a skilled artisan at the time of the instant invention to use topical formulations of nitric oxide synthase inhibitors as first line of choice, with an expectation to produce a local effect.

Wahl et al teaches treatment of chronic inflammatory conditions such as psoriasis (paragraph bridging cols. 3 and 4), by administering the specific nitric oxide synthase inhibitors of the instant claims (see col. 3, lines 39-68). Wahl teaches several routes of administration, including topical application (col. 6, lines 53-65). Thus, Wahl et al teaches the same skin conditions, which have a predisposition to be irritated upon exposure to common cosmetic and pharmaceutical products of Hahn et al, and suggests topical application of nitric oxide synthase inhibitors. Therefore, it would have been obvious for a skilled artisan at the time of the instant invention to use the nitric oxide synthase inhibitors of Wahl (and Williamson et al) in the topical composition of Hahn et al, with an expectation to inhibit the skin irritation caused by the various chemicals (Hahn et al).

Response to Argument

In the Reply Brief, dated 8-21-01, applicants agree that the teachings of Hahn, Williamson et al and Wahl et al are analogous. However, applicants continue to argue that that there is no motivation to combine the references to arrive at the instant invention. Applicants further argue that the cited references employ different mechanisms for treating the symptoms or conditions. Applicants arguments have been considered, but not found to be persuasive because Hahn teaches that the nature of irritation could range from itching, burning, to edema and erythema, which is also seen in inflammation. Thus, the anti-irritant treatment of Hahn et al also applies to the inflammatory conditions (resulting from irritation), the conditions also taught by Williamson et al and Wahl et al.

Applicants also present an analogy of using an antibiotic or a decongestant for the treatment of sinus infection. Based on the analogy, they argue that the treatment of symptoms of disease is not the same as the treatment of the disease itself and therefore, the anti-irritants (treat symptoms) of Hahn cannot be replaced with the anti-inflammatory NO synthase inhibitors (treat disease condition) of Williamson et al or Wahl et al. However, the analogy does not apply to the instant combination of references because Hahn suggests that in addition to being anti-irritant, strontium may act to inhibit or modify the action of other irritation-inducing biological molecules such as eicosanoids or cytokines, that may otherwise may be activated by topical application of skin irritants (col. 5, lines 21-26). Thus, it is apparent from the teachings of Hahn that anti-irritant strontium is not merely treating irritation topically, but is also capable of inhibiting or modifying the cellular mechanisms caused by irritant-induced cytokines i.e, treat the cellular mechanisms that cause the disease condition. While Hahn et al does not specifically

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state NO synthase inhibitors, their teachings include inflammatory conditions such as dermatitis.

Williamson et al recognizes the fact that cytokines induce nitric oxide synthase resulting in the production of large amounts of nitric oxide, which in turn leads to acute and chronic

inflammation (col. 1). Both Williamson et al and Wahl et al teach nitric oxide synthase

inhibitors for the treatment of inflammation. Accordingly, it would have been obvious for a

skilled artisan at the time of the instant invention to add the NO synthase inhibitors of

Williamson et al and Wahl et al, in the anti-irritant containing composition of Hahn et al, with an

expectation to inhibit the NO synthase production caused due to irritation induced cytokines and

thus provide a treatment to inflammatory conditions such as contact dermatitis, atopic dermatitis

etc.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,



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September 19, 2001

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